OUTCOMES OF MITRAL VALVE SURGERY

Peri-operative outcomes of mitral valve surgery at Charlotte Maxeke Johannesburg Academic Hospital

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ABSTRACT

Background: The distribution and determinants of heart disease vary greatly between high-income countries and sub-Saharan Africa where rheumatic heart disease (RHD) is a major public health challenge. Studies from Africa report that RHD is the main cause of cardiovascular morbidity and mortality in the young. Data on mitral valve surgery outcomes in South Africa are limited. The aim of this study was to describe the peri-operative outcomes of patients that have undergone mitral valve surgery at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

Methods: All patients older than 18 years who underwent mitral valve surgery at CMJAH between 1 January 2015 and 31 December 2018 were retrospectively included. Cardiac intensive care records including anaesthesia charts were assessed to describe pre-operative, intra-operative and post-operative data of each patient. Pre-operative data included patient demographics and comorbidities. Intra-operative data included aortic clamp and bypass times. Post-operative variables included outcomes such as sepsis, bleeding, re-operation, and the development of acute kidney injury (AKI). The pre-operative, intra-operative and post-operative outcomes were compared to determine the effect each variable had on post-operative mortality.

Results: Two hundred and seventeen patients underwent mitral valve surgery at CMJAH between 1 January 2015 and 31 December 2018. Four patients' records were incomplete. RHD was found to be the primary aetiology for mitral valve surgery at CMJAH with a mortality rate of 6.1%. Pre-operative findings that contributed to mortality were: EuroSCORE>2%, pre-operative ventilation, dialysis dependence, pre-operative inotropic support, chronic obstructive pulmonary disease, congestive cardiac failure, renal insufficiency, low ejection fraction and New York Heart Association functional class ≥III. Post-operative findings that contributed to increased mortality were prolonged mechanical ventilation, pneumonia, re-operation, AKI, sepsis, bleeding, and transfusion. Increased aortic clamping and cardiopulmonary bypass times increased the risk of prolonged mechanical ventilation, re-operations, pacemaker implantations, AKI, and bleeding.

Conclusions: RHD was found to be the primary aetiology for mitral valve surgery at CMJAH with a mortality of 6.1%. Pre-operative, intra-operative and post-operative predictors of outcomes in this study confirm observations made in other parts of the world.

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INTRODUCTION

Distribution and determinants of heart disease vary greatly between high-income countries and sub-Saharan Africa where rheumatic heart disease (RHD) is a major public health challenge.[1] RHD is the predominant cause of valve disease in Africa,[2] resulting in Africa having the highest prevalence of cardiac disease in children and young adults[1] Cumulative effects of poverty, social instability and lack of infrastructure, resources and awareness contribute to the underestimated impact of RHD.[1, 2] Studies from Africa confirm that RHD is the main cause of cardiac morbidity and mortality from heart surgery.[1-3]

Mitral valve disease, in the form of mitral stenosis and mitral regurgitation, is the commonest form of valve disease and its treatment usually involves surgical repair or replacement. These surgical procedures are highly invasive and not without risk of complications.[3] In South Africa, data on the management and outcomes of mitral valve surgery are limited.[4] Operative mortality in mitral valve replacement surgery is 5% - 6% and 1% - 2% in mitral valve repair.[5] Complications associated with mitral valve surgery are commonly related to cardiopulmonary

bypass (CPB).[6] Platelets are activated and subsequently bind to the exposed subendothelium, the CPB circuit or to the circulating monocytes and neutrophils, resulting in a decrease in platelet numbers.[7] The decrease in platelet numbers and altered platelet function is the rationale behind the major blood loss encountered during cardiac surgery.[7,8]

Multiple studies report that CPB has negative effects on haemostasis and the inflammatory response.[7,9,10] The blood cell activation and plasma protein alteration that occurs during CPB increases bleeding time, post-operative blood loss and increases the risk for massive blood transfusion.[7] Bleeding occurs commonly in cardiac surgery and is a significant cause of morbidity and mortality.[11] Two to eight percent of cardiac reoperations are indicated for uncontrolled bleeding.[11-13] Prolonged cardiopulmonary bypass time (CPBT) was associated with haemostatic abnormalities.[7] CPBT >90 minutes resulted in higher mean blood losses peri-operatively.[7] Re-operation in mitral valve surgery was closely linked to prolonged CPBT.[14] An African study identified CPB >120 minutes was associated with reduction in platelet counts in comparison with CPBT <60 minutes.[15]

In addition to the major blood loss attributed to CPB, there is a significant association with increased CPBT and the development of acute kidney injury (AKI).[16] AKI develops in 2.8% of patients following valvular heart surgery.[6,17] In one study, 38.7% of patients who underwent mitral valve surgery had post-operative AKI, and presented with pre-operative New York Heart Association (NYHA) functional class III and IV, a dilated left ventricle (LV) and low LV ejection fraction (LVEF), all of which lead to hypoperfusion of the kidneys and AKI.[18] AKI prolongs hospital stay and increases the risk of infectious complications and mortality.[17,18] Risk of infection significantly increases with prolonged CPBT.[10,14] Prolonged CPBT resulted in an increased incidence of prolonged mechanical ventilation, increasing the post-operative risk of pneumonia and peri-operative infection.[19] Surgical site infection due to prolonged CPBT ranges from 0.3% - 8%.[20,21] Patients who developed post-operative infection had prolonged CPB and operative times.[20] Shorter operative times, higher haemoglobin (Hb) and higher haematocrit significantly decreased the post-operative risk of infection. The incidence of post-operative infection was 4.5%.[20]

Despite advances in surgical techniques, anaesthesia and critical care, cardiac surgery is associated with high peri-operative risk. Risk stratification scores in cardiac surgery are sophisticated and are used worldwide to determine peri-operative risk.[22] The European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) has been validated in the UK, Europe and North America,[22] and shown to be predictive of peri-operative outcomes in cardiac surgery.[23] However, data from Africa describing the ability of risk scoring systems to predict peri-operative outcomes in African patients undergoing cardiac surgery have not been validated.[22,24] Anaesthesiologists need to assess symptom severity and effort tolerance pre-operatively to determine risk. Advanced NYHA functional class was a risk factor for early mortality.[26,27] Therefore, the aim of this study was to describe the peri-operative outcomes of patients that have undergone mitral valve surgery at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

METHODS

This study was a retrospective, descriptive review of all patients who underwent mitral valve surgery at CMJAH between 1 January 2015 and 31 December 2018. A maximum of 60 patients undergo mitral valve surgery per annum at CMJAH. All patients above the age of 18-years-old were included in the study. Cardiac intensive care unit records including anaesthesia charts were assessed to describe pre-operative, intra-operative and post-operative data of each patient included in the study. Pre-operative data included patient demographics and comorbidities. Intra-operative data included aortic clamp and bypass times. Post-operative variables assessed included outcomes such as sepsis, bleeding, re-operation and the development of AKI. The pre-operative, intra-operative and post-operative outcomes were then compared to determine the effect each variable had on post-operative mortality.

STATA (version 15) was used to analyse the data. Descriptive statistics were used for pre-operative, intra-operative and post-operative data. Categorical variables were described using frequencies and percentages. Inferential statistics were used to compare different variables. A p-value <0.05 was deemed statistically significant. The effect of categorical variables (pre-operative demographics and post-operative outcomes) on mortality were analysed using the Fishers exact test due to the limited sample size. The Shapiro-Wilk test was used to test for the normality of distribution of the continuous variables (aortic clamping and bypass times). As the data was not normally distributed, medians and inter-quartile ranges were used to describe the continuous variables. The two-sample Wilcoxon Rank-Sum Mann-Whitney test was used to compare variables.

Approval (M220343) from the Human Research and Ethics Committee (Medical) and all other relevant authorities was obtained. Data was managed according to the standards stipulated by the University of the Witwatersrand. RedCap® was the data management tool used to obtain information. Each patient was assigned a study number and a separate list of patient details was available only to the researcher.

RESULTS

Two hundred and seventeen patients underwent mitral valve surgery at CMJAH between 1 January 2015 and 31 December 2018. Four of the patients had incomplete records, therefore 213 were included in the study. The pre-operative demographic data of these patients is described in Table 1. One hundred and thirty five patients (63.4%) were female and 78 were male; 86.2% were <60 years of age. A large group of patients, 135 (63.4%) did not have a documented EuroSCORE II. Of those with a documented EuroSCORE II, 71 (91%) had a score <2%, 6 (7.7%) had scores between 2% - 5% and 1 (1.3%) had a score >5%. Patients' pre-operative comorbidities are described in Table II. One hundred and eighty two patients (95.8%) had LVEF >35%. One hundred and fifty two (77.6%) had pulmonary artery pressures (PAP) >30mmHg. RHD was diagnosed in 119 (55.9%) as the primary aetiology for patients undergoing mitral valve surgery. Ischaemic mitral regurgitation (IMR) was diagnosed in 81 (38%) as the main secondary aetiology. Sixty two (29.7%) patients had hypertension, 38 (22.2%) had NYHA functional class ≥III, 31(15%) had previous cardiac surgery, 30 (14.4%) had hypercholesterolaemia and 30 (14.4%) had congestive cardiac failure. Serum creatinine

TABLE I: Pre-operative demographic data of mitral valve surgery patients at CMJAH.

Demographics	Variable	Frequency	Missing data
EuroScore II (%)	<2%	71 (91.03)	135
	2%- 5%	6 (7.69)	
	>5%	1 (1.28)	
Age Group (years)	<60	175 (82.16)	0
	>60	38 (17.84)	
Sex	Male	78 (36.62)	0
	Female	135 (63.38)	
BMI (kg/m²)	<20	1 (0.49)	7
	21-34	196 (95.61)	
	>35	8 (3.90)	

TABLE II: Pre-operative comorbidities.

Cardiac history	Variable	Frequency	Missing data
Previous cardiac surgery	No	177 (85.10)	5
	Yes	31 (14.9)	
Unstable angina	No	204 (99.03)	7
	Yes	2 (0.97)	
LV dysfunction	No	186 (89.86)	6
	Yes	21 (10.14)	
Recent myocardial infarct	No	205 (99.51)	7
	Yes	1 (0.49)	
Hypercholesterolaemia	No	179 (85.65)	4
	Yes	30 (14.35)	
Ischaemic heart disease	No	197 (95.63)	7
	Yes	9 (4.37)	
Hypertension	No	147 (70.33)	9
	Yes	62 (29.67)	
Congestive cardiac failure	No	178 (85.58)	5
	Yes	30 (14.42)	
LVEF	No	8 (4.21)	23
	Yes	182 (95.79)	
Aetiology (primary)	RHD	119 (58.33)	9
	Myxomatous	13 (6.37)	
	Endocarditis	19 (9.31)	
	MV prolapse	28 (13.37)	
	Other	25 (12.25)	
Aetiology (secondary)	IMR (Ischaemic mitral regurgitation)	181 (88.73)	9
	DCMO	4 (1.96)	
	Other	19 (9.31)	
NYHA functional class	< Class III	133 (77.78)	42
	≥ Class III	38 (22.22)	
Smoker	No	190 (91.35)	5
	Yes	18 (8.65)	
COPD	No	194 (92.82)	4
	Yes	15 (7.18)	
Pulmonary arterial pressure (mmHg)	<30	44 (22.45)	17
	>30	152 (77.55)	
Serum creatinine	<110µmol/L	180 (88.24)	9
	>110µmol/L	24 (11.76)	
Kidney disease	No	177 (88.94)	14
	Yes	22 (11.06)	

>110µmol/L was observed in 24 (11.8%) patients, 22 (11.1%) had abnormal renal function, and 21 (10.1%) presented with LV dysfunction. 18 (8.7%) were smokers and 15 (7.2%) presented with pre-operative chronic obstructive pulmonary disease (COPD). Diabetes was present in 21 (10.2%) patients and 9 (4.4%) patients had ischaemic heart disease.

One hundred and five patients (75%) were started on inotropic support and 48 (35.9%) had intra-operative blood transfusions. The mean aortic clamping and bypass time were 97.01 and 144.19 minutes, respectively.

Arrythmias were documented in 113 (54.1%) patients, 41 (19.3%) were transfused post-operatively, and AKI was present in 36 (17%) – Table III. Twenty-eight (18.2%) had significant bleeding and 27 (12.7%) had prolonged mechanical ventilation. Re-operations were done in 26 (12.2%) patients, 26 (12.4%) had pacemakers implanted post-operatively, 24 (11.5%) had sepsis, and cerebrovascular accidents (CVA) were noted in 13 (6.1%) patients. 13 (6.1%) patients died, 9 (4.3%) developed pneumonia and 1 (0.5%) patient had hypertension post-operatively.

Pre-operative data that was associated with mortality included dialysis dependence, pre-operative inotropic support, pre-operative ventilation, LVEF <35%, COPD, NYHA functional class ≥III, renal insufficiency, cardiac failure, and a EuroSCORE II >2% - Table IV. Post-operative features that were independent risk factors for mortality were prolonged mechanical ventilation, re-operation, bleeding, transfusion, AKI, sepsis, and pneumonia – Table V. Results from univariate analysis showed no significant association between aortic clamping time and post-operative outcomes. However, CPBT had a significant influence on post-operative outcomes. Post-operative variables associated with increased CPBT were prolonged mechanical ventilation, re-operation, pacemaker use, AKI and bleeding – Table VI.

TABLE III: Post-operative outcomes not pre-operative outcomes.

Variable	Class	Frequency	Missing data
Arrythmias	No	96 (45.93)	4
	Yes	113 (54.07)	
Prolonged mechanical ventilation	No	185 (87.26)	1
	Yes	27 (12.74)	
Pneumonia	No	202 (95.73)	2
	Yes	9 (4.27)	
CVA	No	199 (93.87)	1
	Yes	13 (6.13)	
Re-operation	No	187 (87.79)	0
	Yes	26 (12.21)	
Pacemaker insertion	No	184 (87.62)	3
	Yes	26 (12.38)	
PAP (pulmonary artery pressure)	No	5 (41.67)	201
	Yes	7 (58.33)	
HPT	No	210 (99.53)	2
	Yes	1 (0.47)	
AKI	No	176 (83.02)	1
	Yes	36 (16.98)	
Sepsis	No	186 (88.57)	3
	Yes	24 (11.53)	
Death	No	200 (93.90)	0
	Yes	13 (6.10)	
Bleeding	No	185 (86.85)	0
	Yes	28 (18.15)	
Transfusion	No	171 (80.66)	1
	Yes	41 (19.34)	

DISCUSSION

Published data approximate the peri-operative mortality rate of mitral valve surgery to be 3%, dependent on the population and the peri-operative risk of the patient prior to surgery.[3,28] In contrast to internationally published data, our peri-operative mortality rate was 6.1%. RHD is the main form of valve heart disease in Africa. Multiple studies across Africa confirm that RHD is the primary cause of morbidity and mortality seen in younger populations undergoing cardiac surgery.[2] Findings from our study are consistent with other data from Africa, where RHD is the primary indication for mitral valve surgery, commonly performed in patients below the age of 60 years.

Advanced age and NYHA class ≥III have been shown to increase peri-operative mortality of valve surgery.[26,27,29] Our study did not show age having a direct effect on peri-operative mortality but confirmed that NYHA class ≥III is an independent risk factor for mortality, likely due to more patients in our study being younger than 60 years and a relatively small sample size. We also found that LVEF <35% was a strong predictor of mortality, confirming the importance of pre-operative echocardiography and functional assessment of the patient. An increase in mortality was noted in patients presenting pre-operatively with COPD, heart failure and need for inotropic support. A limitation of our study is the lack of documentation of the rationale for pre-operative inotropic support. It was

TABLE IV: Association between pre-operative factors and mortality.

Variable	Class	Dead n (%)	Alive n (%)	P-value
EuroScore	< 2 %	1 (1.41)	70 (98.59)	0.020
	2- 5 %	2 (3.33)	4 (66.7)	
	>5 %	0 (0.00)	1 (100.00)	
Pre-operative ventilation	No	8 (3.96)	194 (96.04)	0.028
	Yes	2 (33.33)	4 (66.67)	
Dialysis dependent	No	9 (4.35)	198 (95.65)	0.048
	Yes	1 (100.00)	0 (0.00)	
Pre-operative inotropic support	No	7 (3.45)	196 (96.55)	0.01
	Yes	2 (50.00)	2 (50.00)	
PAP (mmHg)	<30	4 (9.09)	40 (90.91)	0.27
	>30	7 (4.61)	145 (95.39)	
LV dysfunction	No	8 (4.30)	178 (95.70)	0.27
	Yes	2(9.52)	19 (90.48)	
Smoker	No	9 (4.74)	181 (95.26)	0.60
	Yes	1 (5.56)	17 (94.44)	
COPD	No	8 (4.12)	186 (95.88)	0.035
	Yes	3 (20.00)	12 (80.00)	
CCF	No	4 (2.25)	174 (97.75)	0.004
	Yes	5 (16.67)	25 (83.33)	
Renal insufficiency	No	5 (2.82)	172 (97.18)	0.046
	Yes	3 (18.64)	19 (86.36)	
EF%	<35%	2 (25.00)	6 (75.00)	0.03
	>35%	5 (2.75)	177 (97.25)	
Aetiology (primary)	RHD	4 (3.36)	115 (96.64)	0.043
	Myxomatous	0 (0.00)	18 (100.00)	
	Endocarditis	4 (21.05)	15 (78.95)	
	MV prolapse	2 (7.14)	26 (92.86)	
	Other	2 (8.00)	23 (92.00)	
Aetiology (secondary)	IMR	10 (5.52)	171 (94.48)	0.29
	DCMO	1 (25.00)	3 (75.00)	
	Other	1 (5.26)	18 (94.74)	
NYHA	< Class 3	2 (1.50)	131 (98.50)	0.006
	≥Class 3	5 (18.16)	33 (86.84)	

difficult to determine whether inotropic support was an independent risk factor for mortality or if the pre-operative state requiring inotropic support was a greater contributor to the increase noted.

LV dysfunction, atrial fibrillation and pulmonary hypertension are identified risk factors for peri-operative morbidity and mortality.[30] In our study, arrythmias and pulmonary arterial pressures >30mmHg were commonly documented. A limitation of our study is that pulmonary artery pressures were only documented prior to surgery in most patients, making it difficult to assess whether increasing pressures had a direct correlation with the risk of mortality.

TABLE V: Association between post-operative outcomes and mortality.

Variable	Class	Death n (%) n=13 (6.10%)	Alive n (%) n=200 (93.10%)	P-value
Arrythmias	Yes	7 (6.19)	106 (93.81)	1.00
	No	5 (5.21)	91 (94.79)	
Prolonged mechanical ventilation	Yes	10 (37.04)	17 (62.96)	<0.01
	No	2 (1.08)	183 (98.92)	
Pneumonia	Yes	3 (3.33)	6 (66.67)	<0.01
	No	8 (3.96)	194(96.04)	
CVA	Yes	2 (15.38)	11 (84.62)	0.16
	No	10 (5.03)	189 (94.97)	
Re-operation	Yes	9 (34.62)	17 (65.38)	<0.01
	No	4 (2.14)	183(97.86)	
Pacemaker insertion	Yes	1 (3.85)	25 (96.15)	1.00
	No	10 (5.43)	174 (94.57)	
AKI	Yes	7 (19.44)	29 (80.56)	<0.01
	No	5 (2.84)	171 (97.16)	
Sepsis	Yes	7 (29.17)	17 (70.83)	<0.01
	No	3 (1.61)	183 (98.39)	
Bleeding	Yes	8 (28.57)	20 (71.43)	<0.01
	No	5 (2.70)	180 (97.30)	
Transfusion	Yes	8 (19.51)	33 (80.49)	<0.01
	No	4 (2.34)	167 (97.66)	

Risk scoring systems for predicting peri-operative morbidity and mortality are mandatory.[31] There are no risk scoring systems validated in large population groups like sub-Saharan Africa.[22,24] In our study, the EuroSCORE II was used as a pre-operative assessment to predict the risk of mortality. Unfortunately, there were many missing data and very few patient records had a documented EuroSCORE II score. We suggest that a risk scoring system be validated in Africa to assist in predicting mortality in our population.

AKI and its detrimental peri-operative effects during mitral valve surgery have been extensively reviewed.[6,16,17] Patients undergoing mitral valve surgery commonly display a decrease in the volume of blood ejected from the mitral valve due to regurgitation, resulting in poor perfusion to the kidneys. A third of patients who underwent mitral valve surgery developed AKI,[18] and patients presenting with AKI had increased prevalence of hypertension and diabetes. Although patients in our study did not have high rates of hypertension and diabetes, AKI proved to be a major independent predictor of mortality. We also found that increased CPBT of ≥157.5 minutes and aortic clamping times ≥105.5 minutes directly increased the risk of AKI, which is in keeping with prior reports.[6,18,32]

Increased CPBT is an independent risk factor for bleeding and subsequent blood transfusion following cardiac surgery.[7,15] In addition to the above findings, our study confirmed that increased CPBT and aortic clamping times increased the risk of prolonged mechanical ventilation and subsequent pneumonia.[19] A novel finding in our series is the increased use of pacemakers associated with increased bypass and aortic clamping times. Contrary to previous studies, we did not find that sepsis was directly linked to increased CPBT and aortic clamping times. Sepsis, however, was a strong predictor of peri-operative mortality seen in our study.

The economic cost of transfusing blood products and associated complications are high.[33] The limitation in this study is that data on the number of blood products transfused was not collected nor were the negative outcomes of transfusion documented.

TABLE VI: Association between post-operative outcomes and the intra-operative times.

Variable	Class	Aortic clamp time Median (IQR)	P-value	Bypass time Median [IQR]	P-value
Arrythmias	No	91(40.5)	0.37	133(43.5)	0.12
	Yes	98(43)		147(55)	
Prolonged mechanical ventilation	No	91(41)	0.55	137(50.5)	0.029
	Yes	107(51)		156(55)	
Pneumonia	No	92(42)	0.54	140(52)	0.76
	Yes	96.5(53)		141.5(20)	
CVA	No	92(43)	0.92	139(52)	0.28
	Yes	94(37)		151.5(43)	
Re-operation	No	91(41)	0.40	137(53)	0.03
	Yes	106(46)		146.5(66.5)	
Pacemaker insertion	No	91(40)	0.20	136(51)	0.01
	Yes	108(59)		157(57)	
AKI	No	91(42)	0.40	137(52)	0.01
	Yes	105.5(46.5)		157.5(45)	
Sepsis	No	91.5(42.5)	0.98	138(52)	0.36
	Yes	100(33)		147(71)	
Death	No	92(41)	0.66	141(52)	0.30
	Yes	86(63)		150.5(83)	
Bleeding	No	91(42)	0.15	137(51)	0.02
	Yes	106(51)		154(61)	
Transfusion	No	92(40)	0.93	140(52.5)	0.33
	Yes	98(44)		145(53)	

The peri-operative outcomes of mitral valve surgery found in this study can be avoided, anticipated, and effectively managed. A multidisciplinary team of anaesthesiologists, cardiac surgeons, physicians, nurses and allied health professionals are needed to decrease morbidity and assess each patient pre-operatively for the risk of peri-operative mortality.

CONCLUSION

RHD was the predominant primary aetiology for mitral valve surgery in our institution with an overall mortality rate of 6.1%. Pre-operative findings that contributed to increased mortality were EuroSCORE II ≥2%, pre-operative ventilation, dialysis dependence, pre-operative inotropic support, COPD, heart failure, renal insufficiency, LVEF <35% and NYHA ≥III. Post-operative findings that contributed to increased mortality were prolonged mechanical ventilation, pneumonia, reoperation, AKI, sepsis, bleeding, and transfusion. Increased aortic clamping and CPBT significantly increased the risk of prolonged mechanical ventilation, re-operations, use of pacemakers, AKI, and bleeding.

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